

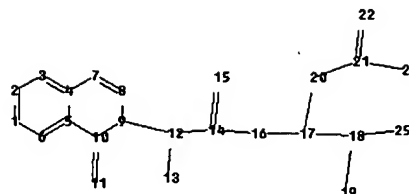
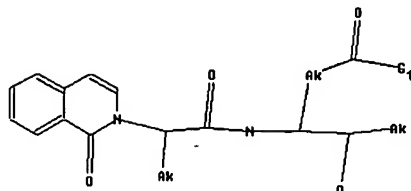
10/743,563(RCE)

***** Welcome to STN International *****
***** STN Columbus *****

FILE 'HOME' ENTERED AT 09:18:38 ON 18 SEP 2006

=> file reg

=>Uploading C:\Program Files\Stnexp\Queries\10743563.str



chain nodes :

11 12 13 14 15 16 17 18 19 20 21 22 24 25

ring nodes :

1 2 3 4 5 6 7 8 9 10

chain bonds :

9-12 10-11 12-13 12-14 14-15 14-16 16-17 17-18 17-20 18-19 18-25 20-21
21-22 21-24

ring bonds :

1-2 1-6 2-3 3-4 4-5 4-7 5-6 5-10 7-8 8-9 9-10

exact/norm bonds :

4-7 5-10 7-8 8-9 9-10 9-12 10-11 12-13 14-15 14-16 16-17 17-20 18-19
18-25 20-21 21-22 21-24

exact bonds :

12-14 17-18

normalized bonds :

1-2 1-6 2-3 3-4 4-5 5-6

isolated ring systems :

containing 1 :

G1:O,N

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:CLASS
19:CLASS 20:CLASS 21:CLASS 22:CLASS 24:CLASS 25:CLASS

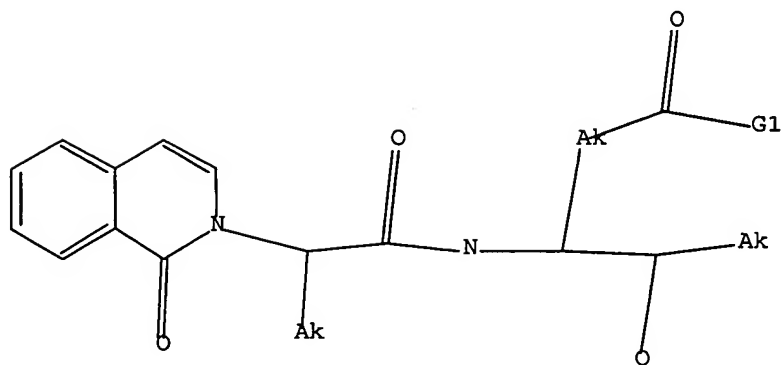
L1 STRUCTURE UPLOADED

=> dis l1

L1 HAS NO ANSWERS

L1 STR

10/743,563(RCE)



G1 O,N

Structure attributes must be viewed using STN Express query preparation.

=> s l1 sam

L2 0 SEA SSS SAM L1

=> s l1 full

L3 2 SEA SSS FUL L1

=> dis l3 1-2

L3 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2006 ACS on STN

RN 640286-58-4 REGISTRY

ED Entered STN: 22 Jan 2004

CN Pentonic acid, 3-[[[(2S)-2-(7-chloro-1-oxo-2(1H)-isoquinolinyl)-1-oxobutyl]amino]-2,3,5-trideoxy-5-fluoro-, 1,1-dimethylethyl ester (9CI)
(CA INDEX NAME)

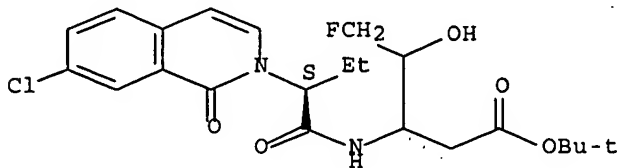
FS STEREOSEARCH

MF C22 H28 Cl F N2 O5

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)

2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2006 ACS on STN

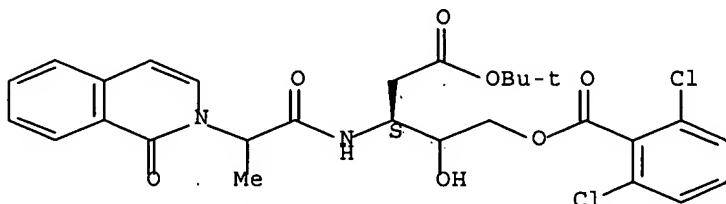
RN 344461-29-6 REGISTRY

ED Entered STN: 03 Jul 2001

10/743,563(RCE)

CN D-glycero-Pentonic acid, 2,3-dideoxy-3-[[1-oxo-2-(1-oxo-2(1H)-
isoquinoliny]propyl]amino]-, 1,1-dimethylethyl ester,
5-(2,6-dichlorobenzoate), (4ξ)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C28 H30 Cl2 N2 O7
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> file caplus

=> s l3

L4 4 L3

=> s l4 and pd<dec 2002

22759844 PD<DEC 2002
(PD<20021200)

L5 1 L4 AND PD<DEC 2002

=> dis l5 bib abs hitstr

L5 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2001:435047 CAPLUS Full-text

DN 135:46192

TI Synthesis and use of heterocyclic substituted-amido halopentanoate
derivatives as caspase inhibitors

IN Golec, Julian; Charifson, Paul; Charrier, Jean-Damien; Binch, Hayley

PA Vertex Pharmaceuticals Incorporated, USA

SO PCT Int. Appl., 88 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001042216	A2	20010614	WO 2000-US33260	20001208 <--
	WO 2001042216	A3	20020228		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,

10/743,563(RCE)

SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2393710 AA 20010614 CA 2000-2393710 20001208 <--
BR 2000016282 A 20020827 BR 2000-16282 20001208 <--
EP 1244626 A2 20021002 EP 2000-988026 20001208 <--

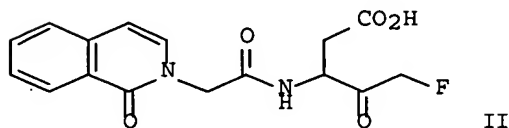
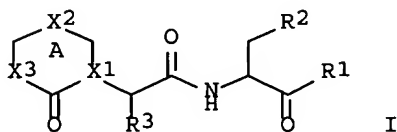
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

JP 2003516393 T2 20030513 JP 2001-543517 20001208
NZ 519424 A 20040326 NZ 2000-519424 20001208
ZA 2002004390 A 20030602 ZA 2002-4390 20020531
NO 2002002656 A 20020806 NO 2002-2656 20020605 <--

PRAI US 1999-169812P P 19991208
WO 2000-US33260 W 20001208

OS MARPAT 135:46192

GI



AB Compds. I and their synthesis are claimed [wherein; R1 = H, CN, CHN2, (substituted)alkyl, aryl, non-aromatic heterocycle, etc.; R2 = CH2COOH, COOH (or ester/amide/isosteres of); R3 = H or alkyl; X1, X3 = N or C; X2 = bond, O, S, N or C wherein any X with suitable valence may bear a substituent; each C in ring A may also be substituted; ring A substituents = H, halo, alkyl, aryl, OH, CN, etc.; A may also bear a fused ring]. Over 20 synthetic examples are given. For instance; substitution of bromoacetic acid Et ester with the corresponding isoquinolone followed by saponification and coupling to 3-amino-5-fluoro-4-hydroxypentanoic acid tert-Bu ester provided the hydroxy ester intermediate. Oxidation of the hydroxy ester followed by treatment with TFA yielded II as a white powder. Compds. of the invention are caspase inhibitors; data is provided for caspase-1, -3, -7 and caspase-8 inhibition (Ki). Also determined was inhibition of IL-1 β secretion from peripheral blood mononuclear cells and activity in a Fas ligand induced apoptosis assay. Compound II had Ki (M-1 s-1) of 248,000 for caspase-1, 130,000 for caspase-3 and an IC50 of 2.9 μ M for IL-1 β secretion. Compds. I may be used as a component of immunotherapy for the treatment of cancer.

IT 344461-29-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(synthesis and use of heterocyclic substituted-amido halopentanoate derivs. as caspase inhibitors)

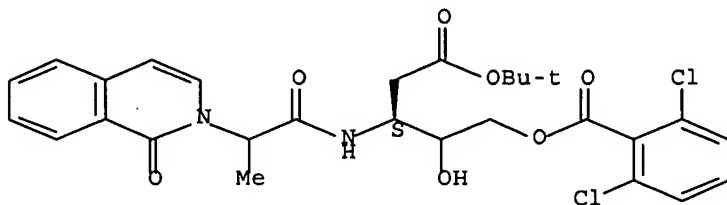
RN 344461-29-6 CAPLUS

CN D-glycero-Pentonic acid, 2,3-dideoxy-3-[[1-oxo-2-(1-oxo-2(1H)-

10/743,563(RCE)

isoquinolinyl)propyl]amino]-, 1,1-dimethylethyl ester,
5-(2,6-dichlorobenzoate), (4ξ)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



=> dis his

(FILE 'HOME' ENTERED AT 09:18:38 ON 18 SEP 2006)

FILE 'REGISTRY' ENTERED AT 09:18:55 ON 18 SEP 2006

L1 STRUCTURE UPLOADED
L2 0 S L1 SAM
L3 2 S L1 FULL

FILE 'CAPLUS' ENTERED AT 09:19:32 ON 18 SEP 2006

L4 4 S L3
L5 1 S L4 AND PD<DEC 2002

=> s l4 not l5

L6 3 L4 NOT L5

=> dis l6 1-3 bib abs

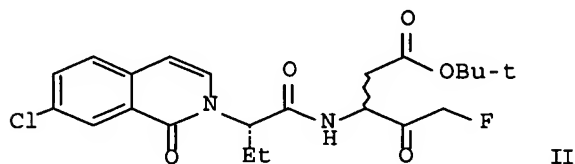
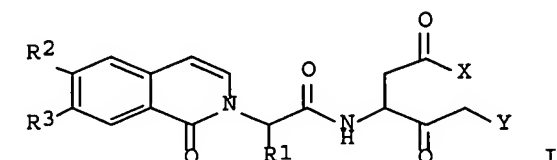
L6 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:565214 CAPLUS Full-text
DN 141:106388
TI Preparation of 4-oxo-3-(1-oxo-1H-isoquinolin-2-ylacetyl-amino)-pentanoic
acid ester and amide derivatives as caspase inhibitors
IN Charrier, Jean-Damien; Mortimore, Michael; Studley, John R.
PA Vertex Pharmaceuticals Incorporated, USA
SO PCT Int. Appl., 104 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004058718	A1	20040715	WO 2003-US40870	20031222
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW			
	RW:	BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK,			

10/743,563(RCE)

TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2511235	AA	20040715	CA 2003-2511235	20031222
AU 2003303345	A1	20040722	AU 2003-303345	20031222
US 2004192612	A1	20040930	US 2003-743563	20031222
EP 1581501	A1	20051005	EP 2003-814289	20031222
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CN 1745065	A	20060308	CN 2003-80109285	20031222
JP 2006513220	T2	20060420	JP 2004-563916	20031222
PRAI US 2002-435133P	P	20021220		
WO 2003-US40870	W	20031222		
OS MARPAT 141:106388				
GI				



AB The title compds. of formula I [X = alkoxy, (substituted) NH₂, etc.; Y = halo, trifluorophenoxy, tetrafluorophenoxy; R₁ = alkyl; R₂, R₃ = H, halo, OCF₃, CN, CF₃] are prepared. The present invention also provides pharmaceutical compns. and methods using such compns. for treating a caspase-mediated disease, particularly in the central nervous system. Thus, II was prepared from 7-chloroisochromen-1-one (preparation given), (S)-2-aminobutyric acid tert-Bu ester and 3-amino-5-fluoro-4-hydroxypentanoic acid tert-Bu ester.

L6 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2004:20662 CAPLUS Full-text

DN 140:77410

TI Preparation of isoquinolinone and quinazolinone peptide derivatives as caspase inhibitors

IN Knegt, Ronald; Mortimore, Michael; Studley, John; Millan, David

PA Vertex Pharmaceuticals Incorporated, USA

SO PCT Int. Appl., 95 pp.

CODEN: PIXXD2

DT Patent

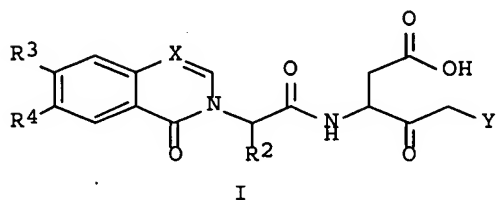
LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-----	---	----	-----	-----
PI	WO 2004002961	A1	20040108	WO 2003-US20557	20030627
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,				

LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
 PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA,
 UG, US, UZ, VN, YU, ZA, ZM, ZW
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
 KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
 FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
 BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2493646	AA	20040108	CA 2003-2493646	20030627
AU 2003248758	A1	20040119	AU 2003-248758	20030627
US 2004072850	A1	20040415	US 2003-609147	20030627
BR 2003012232	A	20050510	BR 2003-12232	20030627
EP 1539701	A1	20050615	EP 2003-762231	20030627
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2005533825	T2	20051110	JP 2004-518103	20030627
NO 2005000851	A	20050329	NO 2005-851	20050217
PRAI US 2002-392592P	P	20020628		
US 2002-435073P	P	20021220		
WO 2003-US20557	W	20030627		
OS MARPAT 140:77410				
GI				



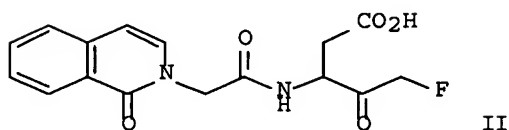
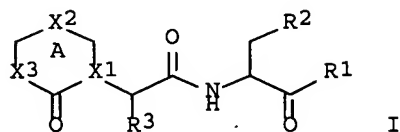
AB The invention relates to isoquinolinones and quinazolinones I [X is CH or N; Y is halo, tri- or tetrafluorophenoxy; R2 is alkyl; R3 is H, halo, OCF3, CN, or CF3; R4 is groups R3 or alkylthio, (un)substituted Ph, phenoxy, or phenylthio; with the proviso that when Y is halo, then R3 and R4 are not both H] which are caspase inhibitors useful in compns. for the treatment of various diseases, conditions, or disorders. Thus, I (X = CH, Y = F, R2 = Et, R3 = H, R4 = Cl), prepared by coupling of (S)-2-(7-chloro-1-oxo-1H-isoquinolin-2-yl)butyric acid (preparation given) with 3-amino-5-fluoro-4-hydroxypentanoic acid tert-Bu ester, had Ki (M-1 s-1) > 500,000 for inhibition of caspase-1 or caspase-3, Ki 100,000-500,000 for inhibition of caspase-8, and IC50 < 1 µM for inhibition of interleukin-1β secretion.

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN
 AN 2003:991174 CAPLUS Full-text
 DN 140:28050
 TI Synthesis of peptide heterocyclic derivatives as caspase inhibitors
 IN Golec, Julian M. C.; Charifson, Paul S.; Charrier, Jean-Damien; Binch, Hayley
 PA UK
 SO U.S. Pat. Appl. Publ., 28 pp.
 CODEN: USXXCO
 DT Patent
 LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003232846	A1	20031218	US 2002-166437	20020610
PRAI	US 2002-166437		20020610		
OS	MARPAT 140:28050				
GI					



AB Compds. I and their synthesis are claimed [R1 = H, CN, CHN2, (substituted)alkyl, aryl, non-aromatic heterocycle, etc.; R2 = CH2COOH, CO2H (or ester/amide/isosteres of); R3 = H or alkyl; X1, X3 = N or C; X2 = bond, O, S, N or C wherein any X with suitable valence may bear a substituent; each C in ring A may also be substituted; ring A substituents = H, halo, alkyl, aryl, OH, CN, etc.; A may also bear a fused ring]. Over 20 synthetic examples are given. Thus, substitution of bromoacetic acid Et ester with the corresponding isoquinolone followed by saponification and coupling to 3-amino-5-fluoro-4-hydroxypentanoic acid tert-Bu ester provided the hydroxy ester intermediate. Oxidation of the hydroxy ester followed by treatment with TFA yielded II as a white powder. Compds. of the invention are caspase inhibitors; data is provided for caspase-1, -3, -7 and caspase-8 inhibition (Ki). Also determined was inhibition of IL-1 β secretion from peripheral blood mononuclear cells and activity in a Fas ligand induced apoptosis assay. Compound II had Ki (M-1 s-1) of 248,000 for caspase-1, 130,000 for caspase-3 and an IC50 of 2.9 μ M for IL-1 β secretion. Compds. I may be used as a component of immunotherapy for the treatment of cancer.

=> log y

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

16.20

187.15

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE

TOTAL

ENTRY

SESSION

CA SUBSCRIBER PRICE

-3.00

-3.00

STN INTERNATIONAL LOGOFF AT 09:20:49 ON 18 SEP 2006